A MAPK Signaling Pathway Leading To WRKY29 Induction

Flg22 → Receptor →

AtMEKK1 ⇌ AtMEKK1★

AtMKK 4/5 ⇌ (P)-AtMKK 4/5

AtMPK 3/6 ⇌ (P)-AtMPK 3/6

Transcription Factor   Inactive   Active → WRKY29

FIGURE 1

WRKY29

WRKY
domain

NLS

~ 60 a.a.

304

---WRKY-----C----C-------H--H---
(Trp-Arg-Lys-Tyr)   Zinc-finger motif
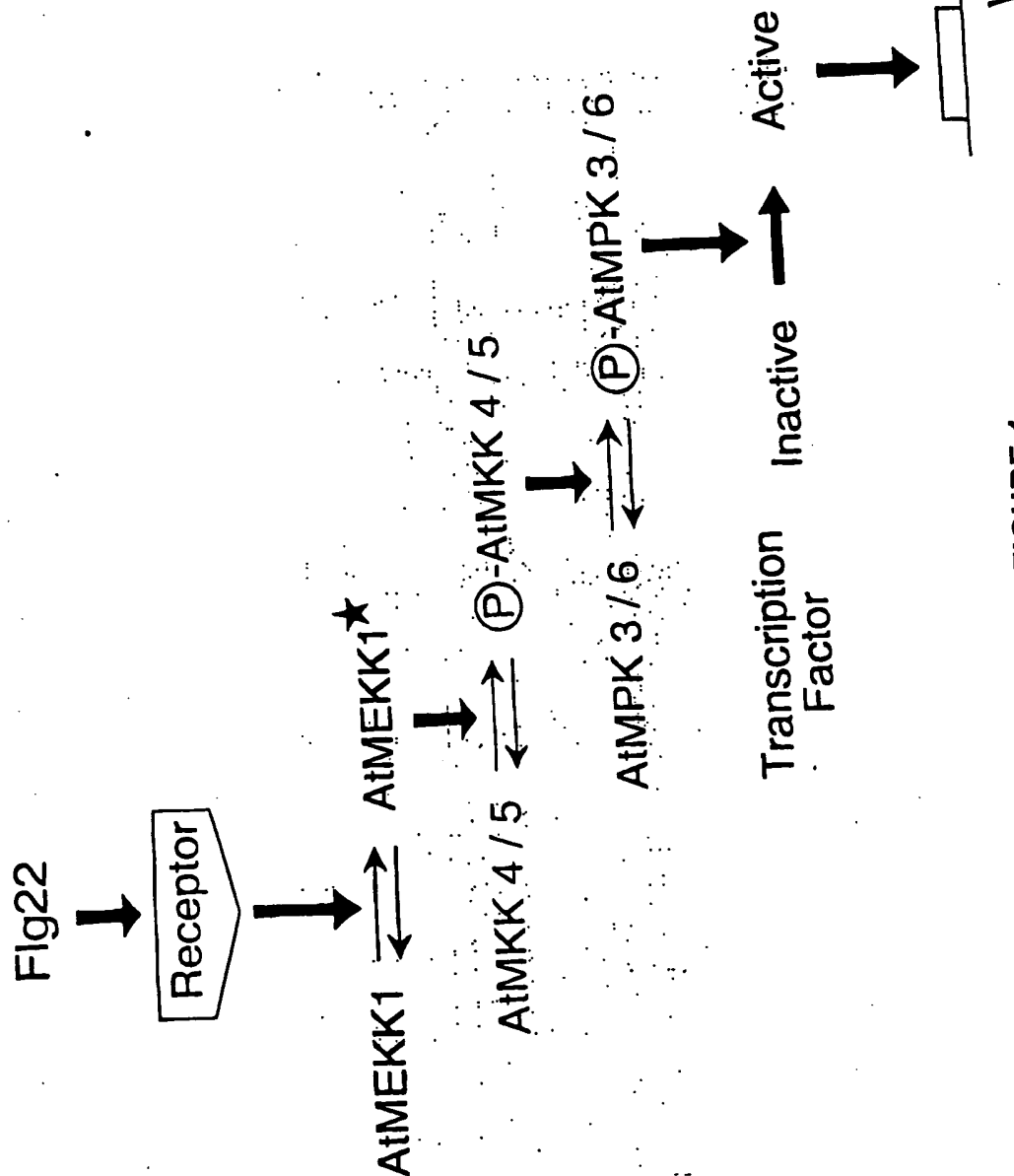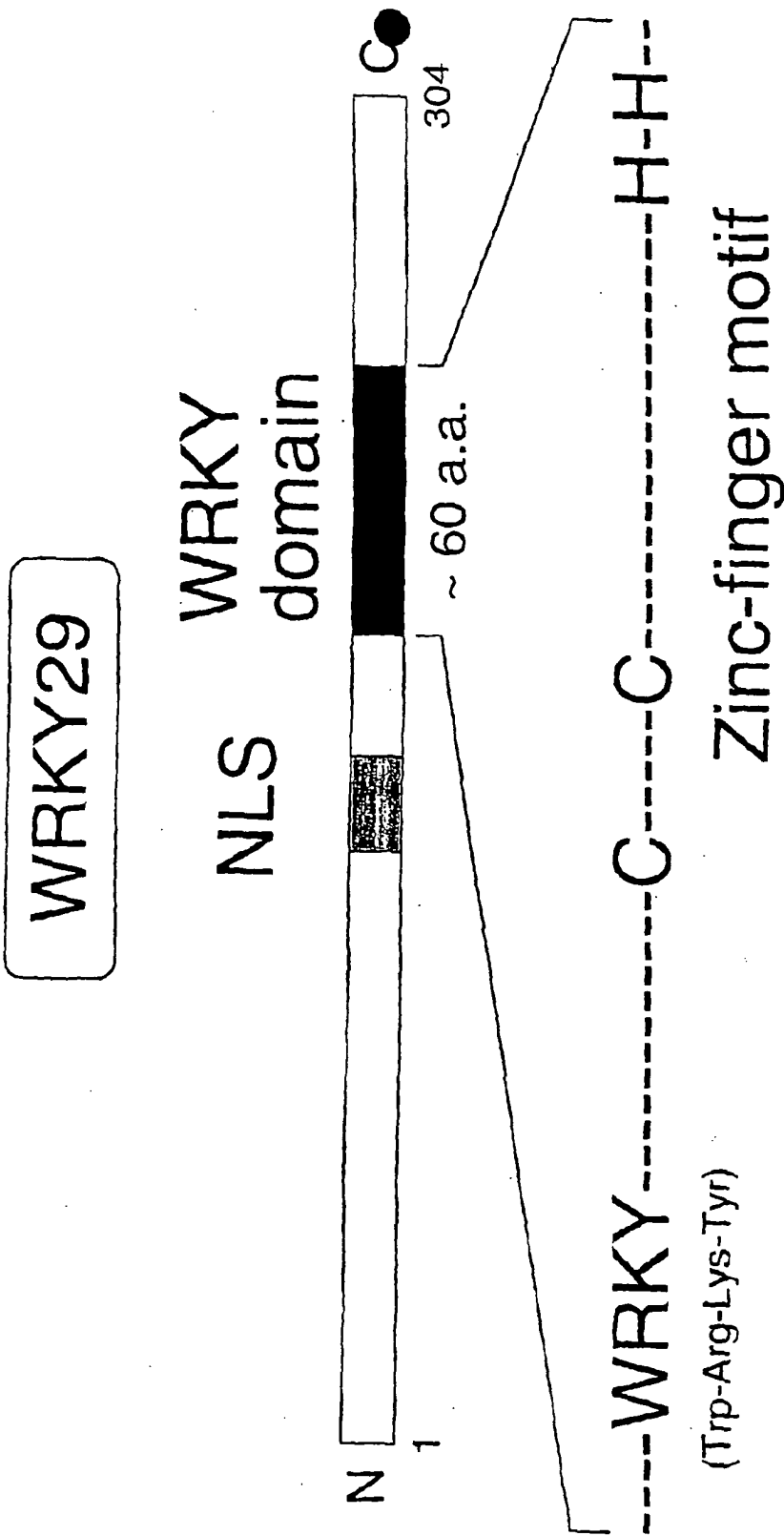
Target Sequence : W box
(T)(T)TGAC(C/T)

FIGURE 2

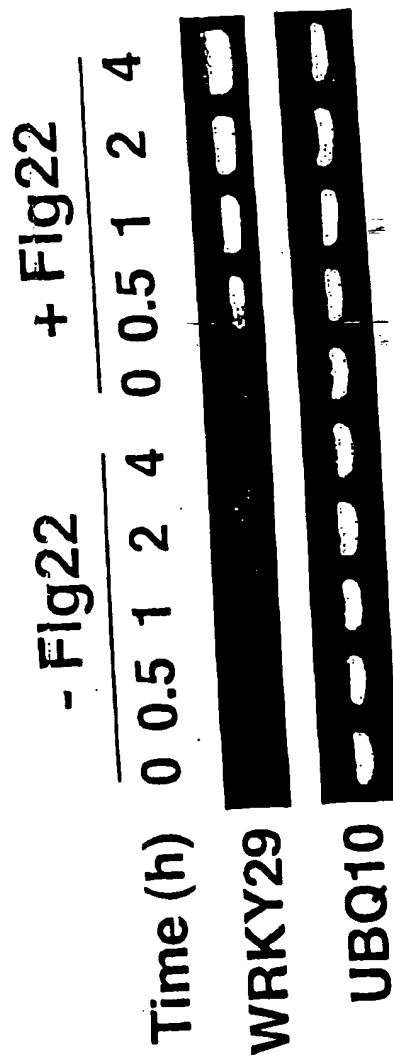Flg22 Induces WRKY29
in Arabidopsis Protoplasts
(RT-PCR Analysis)

FIGURE 3

MKK4 (cDNA accession number: AB015315)

*Wild-type cDNA sequence from start to end codons
(1101 base pairs including the end TAG):*

atgagaccgattcaatcgcctccaggagtttccgttccggtgaaaagccgtccccgtcg
ccgtcctgatcttaccttaccgcttcctcaacgcgatgtttctctcgctgtacctcttc
ctctcccacctacttccggtggttccggtggctctagtggatctgcgccgtcttctggt
ggttcggcgtcttcaacgaacactaacagctccatagaagcgaagaactattcggattt
agtgagaggtaaccgtatcggaagcggagcaggtggaacggtatacaaagtgattcacc
gtccgagttctcgtctatatgcacttaaggtgatatacggtaaccacgaggagactgtg
agacgtcagatctgtagagagatcgagattttacgagatgtgaatcatccaaacgttgt
gaaatgtcacgagatgtttgatcagaacggtgagatccaggttttgcttgagtttatgg
ataaaggttctttagaaggtgctcatgtgtggaaagagcaacaattagctgatctatct
cgtcagattcttagtggtttagcttatctccatagccgtcacatagttcatcgtgatat
caaaccatcgaatcttttgataaactctgctaaaaacgttaagattgctgattttggag
ttagtaggatcttggctcag**tatggatccgtgtaat**catctgttggaaccattgct
tatatgagtcctgagaggattaacactgatttgaatcagggaaagtatgatggttatgc
tggagatatttggagcttaggtgttagcattttggagttttacttgggggaggtttcctt
tccctgtgagtagacaaggtgattgggctagtcttatgtgtgccatttgtatgtctcag
cctccagaagctccagcgactgcgtcgccggagtttcggcattttatctcgtgttgctt
gcagagagaaccggggaaaaggaggagtgctatgcagctattgcagcatcctttcatat
taagagcaagtccgagccagaacaggtctcctcagaatctacatcaactcttgcctcct
cctcgtcctctgtcctcgtcttcttctccaaccaca**tag** (SEQ ID NO.:3)

Wild-type protein sequence (366 aminoacids):

MRPIQSPPGVSVPVKSRPRRRPDLTLPLPQRDVSLAVPLPLPPTSGGSGGSSGSAPSSG
GSASSTNTNSSIEAKNYSDLVRGNRIGSGAGGTVYKVIHRPSSRLYALKVIYGNHEETV
RRQICREIEILRDVNHPNVVKCHEMFDQNGEIQVLLEFMDKGSLEGAHVWKEQQLADLS
RQILSGLAYLHSRHIVHRDIKPSNLLINSAKNVKIADFGVSRILAQ**M**DPCN**S**SVGTIA
YMSPERINTDLNQGKYDGYAGDIWSLGVSILEFYLGRFPFPVSRQGDWASLMCAICMSQ
PPEAPATASPEFRHFISCCLQREPGKRRSAMQLLQHPFILRASPSQNRSPQNLHQLLPP
PRPLSSSSSPTT   (SEQ ID NO.:4)

FIGURE 4

Mutations rendering MKK4 constitutively active:

- modify Serine (S) 230 to Glutamic Acid (E) by changing codon TCA into GAA

The mutations were done by PCR using the primers (mutated base pairs in lower case, both are from 5' end to 3' end):

CTTGGCTCAG▮▮TATGGATCCGTGTAATgaATCTGTTGGAAC
TCCAACAGATtcATTACACGGATCCATA▮CTGAGCCAAG   (SEQ ID NO.3)

So the sequences after mutations are:

> *MKK4act mutant sequence from ▮start▮ to ▮end▮ codons*
> *(1101 base pairs including the end TAG):*

atgagaccgattcaatcgcctccaggagtttccgttccggtgaaaagccgtccccgtcgccgtcctgatct
taccttaccgcttcctcaacgcgatgtttctctcgctgtacctcttcctctcccacctacttccggtggtt
ccggtggctctagtggatctgcgccgtcttctggtggttcggcgtcttcaacgaacactaacagctccata
gaagcgaagaactattcggatttagtgagaggtaaccgtatcggaagcggagcaggtggaacggtatacaa
agtgattcaccgtccgagttctcgtctatatgcacttaaggtgatatacggtaaccacgaggagactgtga
gacgtcagatctgtagagagatcgagattttacgagatgtgaatcatccaaacgttgtgaaatgtcacgag
atgtttgatcagaacggtgagatccaggttttgcttgagtttatggataaaggttctttagaaggtgctca
tgtgtggaaagagcaacaattagctgatctatctcgtcagattcttagtggtttagcttatctccatagcc
gtcacatagttcatcgtgatatcaaaccatcgaatcttttgataaactctgctaaaaacgttaagattgct
gattttggagttagtaggatcttggctcag▮▮tatggatccgtgtaatgaatctgttggaaccattgctta
tatgagtcctgagaggattaacactgatttgaatcagggaaagtatgatggttatgctggagatatttgga
gcttaggtgttagcattttggagttttacttggggaggtttcctttccctgtgagtagacaaggtgattgg
gctagtcttatgtgtgccatttgtatgtctcagcctccagaagctccagcgactgcgtcgccggagtttcg
gcattttatctcgtgttgcttgcagagagaaccggggaaaaggaggagtgctatgcagctattgcagcatc
ctttcatattaagagcaagtccgagccagaacaggtctcctcagaatctacatcaactcttgcctcctcct
cgtcctctgtcctcgtcttcttctccaaccaca**tag** (SEQ ID NO.:6)

> *MKK4act mutant protein sequence (366 aminoacids):*

MRPIQSPPGVSVPVKSRPRRRPDLTLPLPQRDVSLAVPLPLPPTSGGSGGSSGSAPSSGGSASSTNTNSSI
EAKNYSDLVRGNRIGSGAGGTVYKVIHRPSSRLYALKVIYGNHEETVRRQICREIEILRDVNHPNVVKCHE
MFDQNGEIQVLLEFMDKGSLEGAHVWKEQQLADLSRQILSGLAYLHSRHIVHRDIKPSNLLINSAKNVKIA
DFGVSRILAQ▮MDPCN▮SVGTIAYMSPERINTDLNQGKYDGYAGDIWSLGVSILEFYLGRFPFPVSRQGDW
ASLMCAICMSQPPEAPATASPEFRHFISCCLQREPGKRRSAMQLLQHPFILRASPSQNRSPQNLHQLLPPP
RPLSSSSSPTT (SEQ ID NO.:7)

FIGURE 5

MKK5 (cDNA accession number: AB015316)

*Wild-type cDNA sequence from start to end codons
(1047 base pairs including the end TAG):*

atgaaaccgattcaatctccttctggagtagcttcacctatgaagaaccgtttacgcaa
acgtcctgacctaagcttaccactcccacaccgcgacgtcgctctcgccgtacctctcc
ctctcccacctccttcttcctcttcatccgctccggcgtcttcctccgcgatctcaacc
aacatctccgccgctaaaagcttatccgagctagaacgagtgaaccgaatcggaagcgg
agccggaggaacggtttacaaagtaatccacactccgacgtcacgtcctttcgctctca
aagtgatttacggaaaccacgaagataccgtgagacgtcagatctgtagagagatcgag
atcttaagaagtgttgatcatccaaacgttgtgaaatgtcacgatatgtttgatcataa
cggtgagatccaggttttgcttgagtttatggatcaaggatctcttgaaggagctcata
tatggcaagaacaggaattagctgatctctctcgtcagattcttagtggattagcttat
cttcatcgtcgtcatatcgttcatcgtgatatcaaaccttcgaatctccttataaactc
agctaaaaatgtgaaaattgctgattttggtgtgagtaggatcttggcacaa█aatgg
atccttgtaat█catctgttggtactattgcttatatgagtcctgagaggattaatact
gatttgaatcatggtcgttacgatggttatgctggagatgtttggagtttaggtgttag
tatcttggagtttacttggggaggtttccttttgctgtgagtagacaaggtgattggg
ctagtcttatgtgtgctatttgtatgtctcagccacctgaagctccggctacggcgtct
caggagtttcgtcactttgtttcttgttgtttacagagtgatcctcctaagagatggtc
agctcaacagcttttgcagcatcctttcatacttaaagctaccggtggtcctaatctcc
gtcaaatgttgccgccgcctcgtcctcttccttctgcctct**tag** (SEQ ID NO.:8)

Wild-type protein sequence (348 aminoacids):

MKPIQSPSGVASPMKNRLRKRPDLSLPLPHRDVALAVPLPLPPPSSSSSAPASSSAIST
NISAAKSLSELERVNRIGSGAGGTVYKVIHTPTSRPFALKVIYGNHEDTVRRQICREIE
ILRSVDHPNVVKCHDMFDHNGEIQVLLEFMDQGSLEGAHIWQEQELADLSRQILSGLAY
LHRRHIVHRDIKPSNLLINSAKNVKIADFGVSRILAQ█MDPCN█SVGTIAYMSPERINT
DLNHGRYDGYAGDVWSLGVSILEFYLGRFPFAVSRQGDWASLMCAICMSQPPEAPATAS
QEFRHFVSCCLQSDPPKRWSAQQLLQHPFILKATGGPNLRQMLPPPRPLPSAS   (SEQ
ID NO.:9)

FIGURE 6

Mutations rendering MKK5 constitutively active:

- modify Threonine (T) 215 To Glutamic Acid (E) by changing codon ACA into GAA

- modify Serine (S) 221 to Glutamic Acid (E) by changing codon TCA into GAA

The mutations were done by PCR using the primers (mutated base pairs in lower case, both are from 5' end to 3' end):

CTTGGCACAAgaAATGGATCCTTGTAATgaATCTGTTGGT
ACCAACAGATtcATTACAAGGATCCATT■TTGTGCCAAG   (SEQ ID NO.:10)

So the sequences after mutations are:

MKK5act mutant cDNA sequence from start to end codons (1047 base pairs including the end TAG):

atgaaaccgattcaatctccttctggagtagcttcacctatgaagaaccgtttacgcaa
acgtcctgacctaagcttaccactcccacaccgcgacgtcgctctcgccgtacctctcc
ctctcccacctccttcttcctcttcatccgctccggcgtcttcctccgcgatctcaacc
aacatctccgccgctaaaagcttatccgagctagaacgagtgaaccgaatcggaagcgg
agccggaggaacggtttacaaagtaatccacactccgacgtcacgtcctttcgctctca
aagtgatttacggaaaccacgaagataccgtgagacgtcagatctgtagagagatcgag
atcttaagaagtgttgatcatccaaacgttgtgaaatgtcacgatatgtttgatcataa
cggtgagatccaggttttgcttgagtttatggatcaaggatctcttgaaggagctcata
tatggcaagaacaggaattagctgatctctctcgtcagattcttagtggattagcttat
cttcatcgtcgtcatatcgttcatcgtgatatcaaaccttcgaatctccttataaactc
agctaaaaatgtgaaaattgctgattttggtgtgagtaggatcttggcacaa■aatgg
atccttgtaatgaatctgttggtactattgcttatatgagtcctgagaggattaatact
gatttgaatcatggtcgttacgatggttatgctggagatgtttggagtttaggtgttag
tatcttggagtttttacttggggaggtttccttttgctgtgagtagacaaggtgattggg
ctagtcttatgtgtgctatttgtatgtctcagccacctgaagctccggctacggcgtct
caggagtttcgtcactttgtttcttgttgtttacagagtgatcctcctaagagatggtc
agctcaacagcttttgcagcatcctttcatacttaaagctaccggtggtcctaatctcc
gtcaaatgttgccgccgcctcgtcctcttccttctgcctcttag (SEQ ID
NO.:11)

MKK5act mutant protein sequence (348 aminoacids):

MKPIQSPSGVASPMKNRLRKRPDLSLPLPHRDVALAVPLPLPPPSSSSSAPASSSAIST
NISAAKSLSELERVNRIGSGAGGTVYKVIHTPTSRPFALKVIYGNHEDTVRRQICREIE
ILRSVDHPNVVKCHDMFDHNGEIQVLLEFMDQGSLEGAHIWQEQELADLSRQILSGLAY
LHRRHIVHRDIKPSNLLINSAKNVKIADFGVSRILAQ■MDPCNESVGTIAYMSPERINT
DLNHGRYDGYAGDVWSLGVSILEFYLGRFPFAVSRQGDWASLMCAICMSQPPEAPATAS
QEFRHFVSCCLQSDPPKRWSAQQLLQHPFILKATGGPNLRQMLPPPRPLPSAS   (SEQ
ID NO.:12)

FIGURE 7

Alignment of MKK4 and MKK5 wild-type:

```
MKK4  MRPIQSPPGVSVPVKSRPRRRPDLTLPLPQRDVSLAVPLPLPPTSGGSGG
MKK5  MKPIQSPSGVASPMKNRLKRPDLSLPLPHRDVALAVPLPLPPPS-----

MKK4  SSGSAPSSGGSASSTNTNSSIEAKNYSDLVRGNRIGSGAGGTVYKVIHRP
MKK5  SSSSAPASS-SAISTNIS---AAKSLSELERVNRIGSGAGGTVYKVIHTP

MKK4  SSRLYALKVIYGNHEETVRRQICREIEILRDVNHPNVVKCHEMFDQNGEI
MKK5  TSRPFALKVIYGNHEDTVRRQICREIEILRSVDHPNVVKCHDMFDHNGEI

MKK4  QVLLEFMDKGSLEGAHVWKEQQLADLSRQILSGLAYLHSRHIVHRDIKPS
MKK5  QVLLEFMDQGSLEGAHIWQEQELADLSRQILSGLAYLHRRHIVHRDIKPS

MKK4  NLLINSAKNVKIADFGVSRILAQ MDPCN SVGTIAYMSPERINTDLNQG
MKK5  NLLINSAKNVKIADFGVSRILAQ MDPCN SVGTIAYMSPERINTDLNHG

MKK4  KYDGYAGDIWSLGVSILEFYLGRFPFPVSRQGDWASLMCAICMSQPPEAP
MKK5  RYDGYAGDVWSLGVSILEFYLGRFPFAVSRQGDWASLMCAICMSQPPEAP

MKK4  ATASPEFRHFISCCLQREPGKRRSAMQLLQHPFILRASPSQNRSPQNLHQ
MKK5  ATASQEFRHFVSCCLQSDPPKRWSAQQLLQHPFILKATG----GP-NLRQ

MKK4  LLPPPRPLSSSSSPTT      (SEQ ID NO.:13)
MKK5  MLPPPRPLPSAS----      (SEQ ID NO.:14)
```
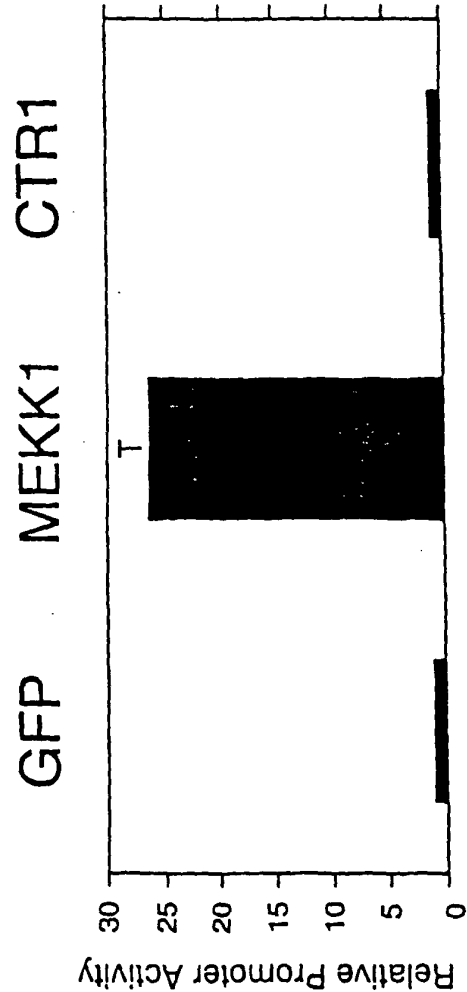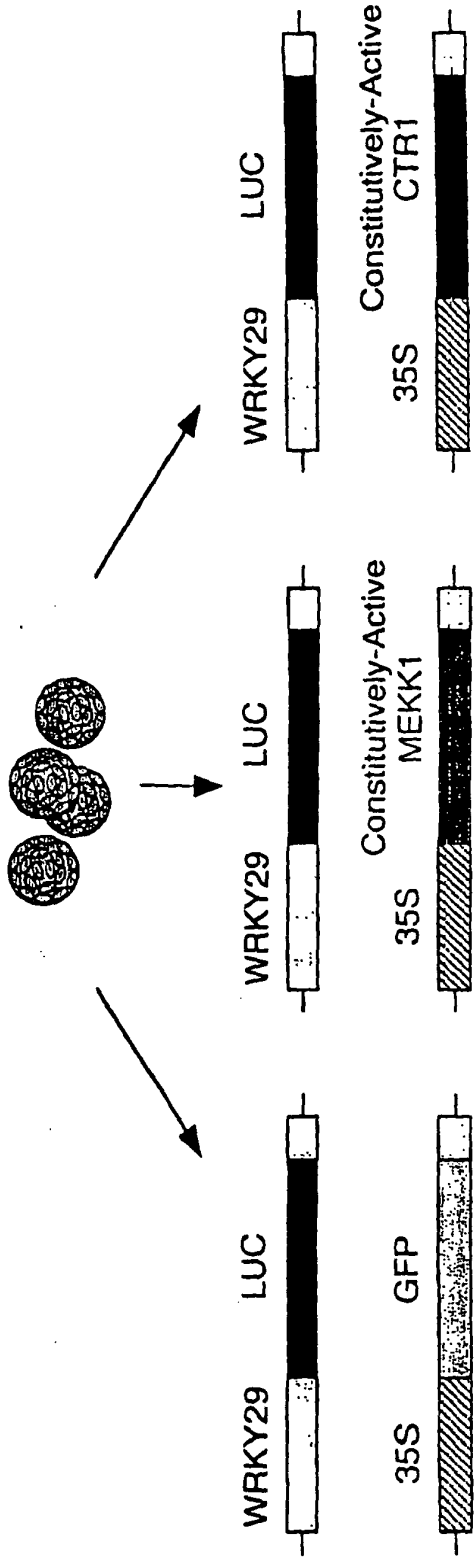
FIGURE 8

Title: MASTER ACTIVATORS OF PATHOGEN
RESPONSIVE GENES
Applicants: Jen Sheen, et al.
Filing Date: September 12, 2003
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Serial Not: Not Yet Assigned
Customer No.: 21559

FIGURE 9

FIGURE 10

Title: MASTER ACTIVATORS OF PATHOGEN
RESPONSIVE GENES
Applicants: Jen Sheen, et al.
Filing Date: September 12, 2003
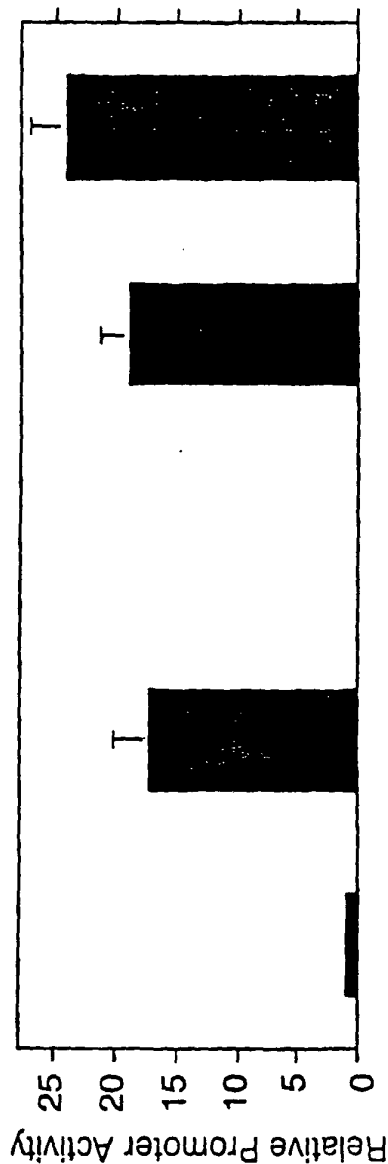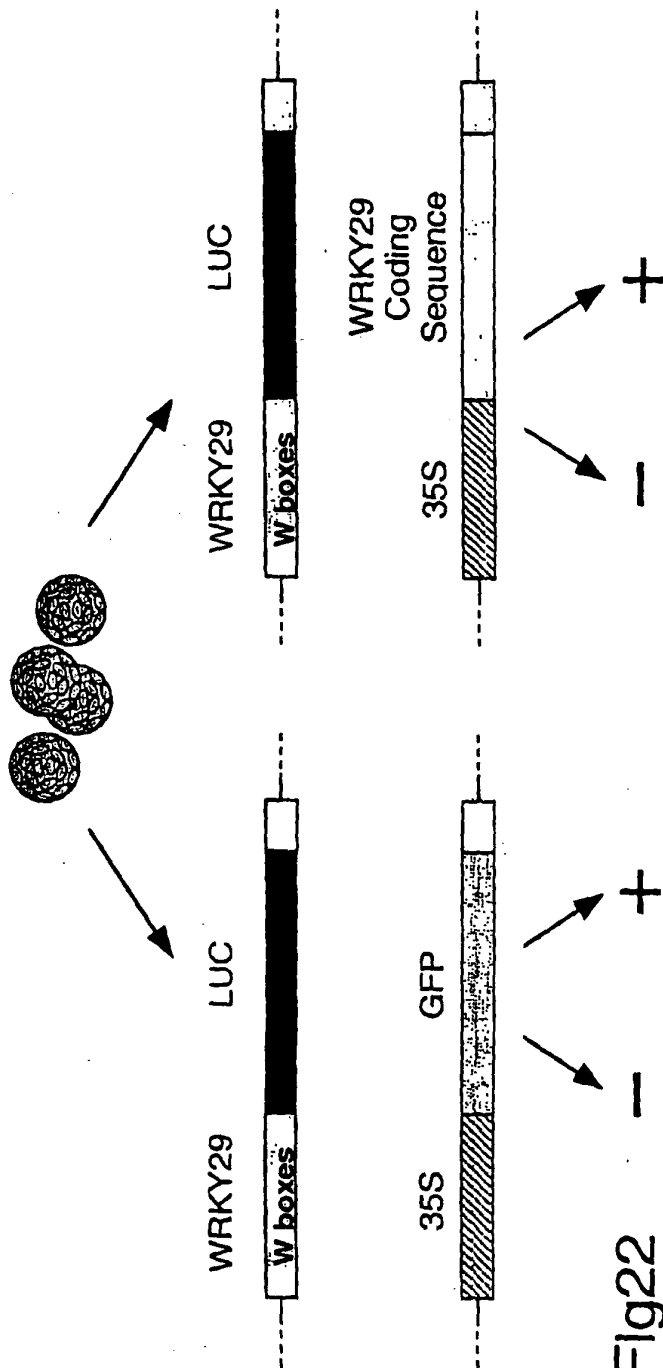Page 11 of 22

Serial Not: Not Yet Assigned
Customer No.: 21559
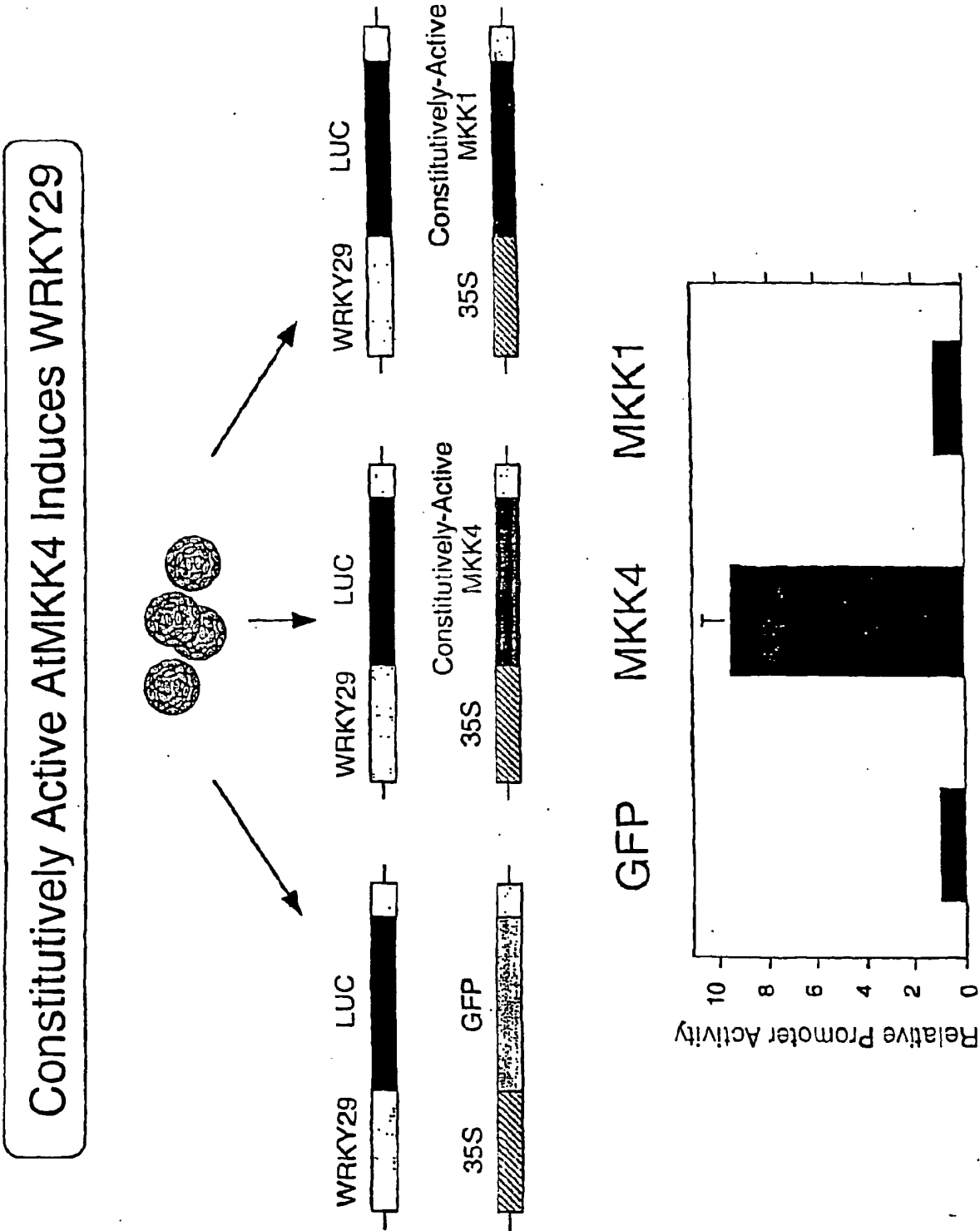
FIGURE 11

WRKY29 Regulates Early Defense Genes
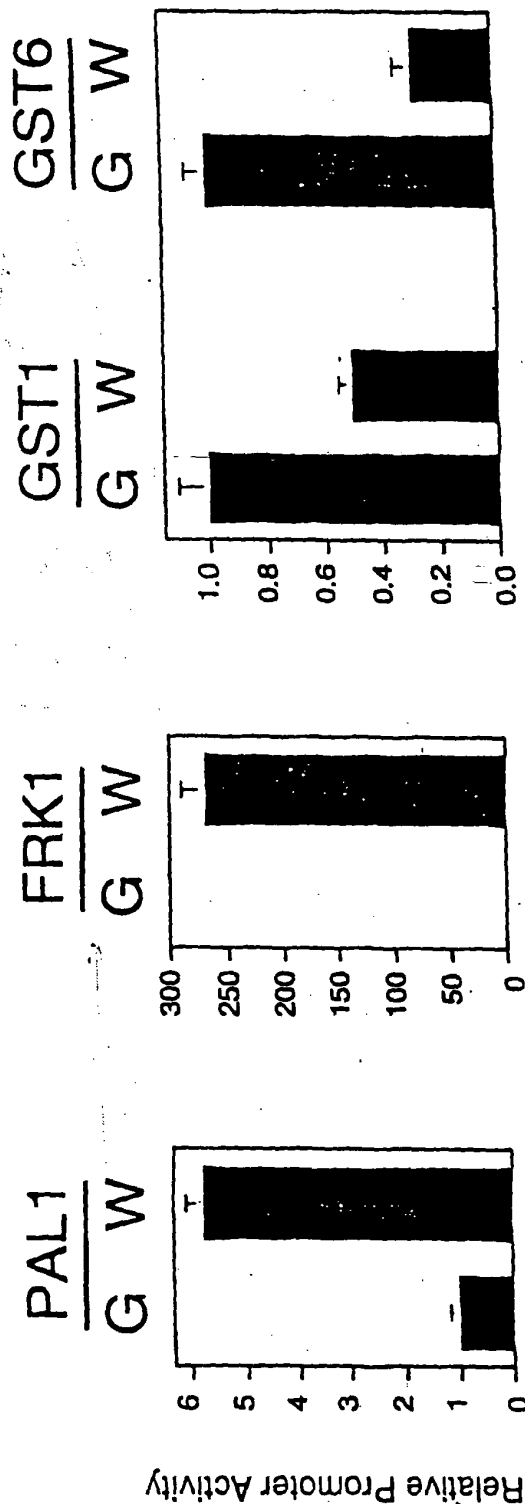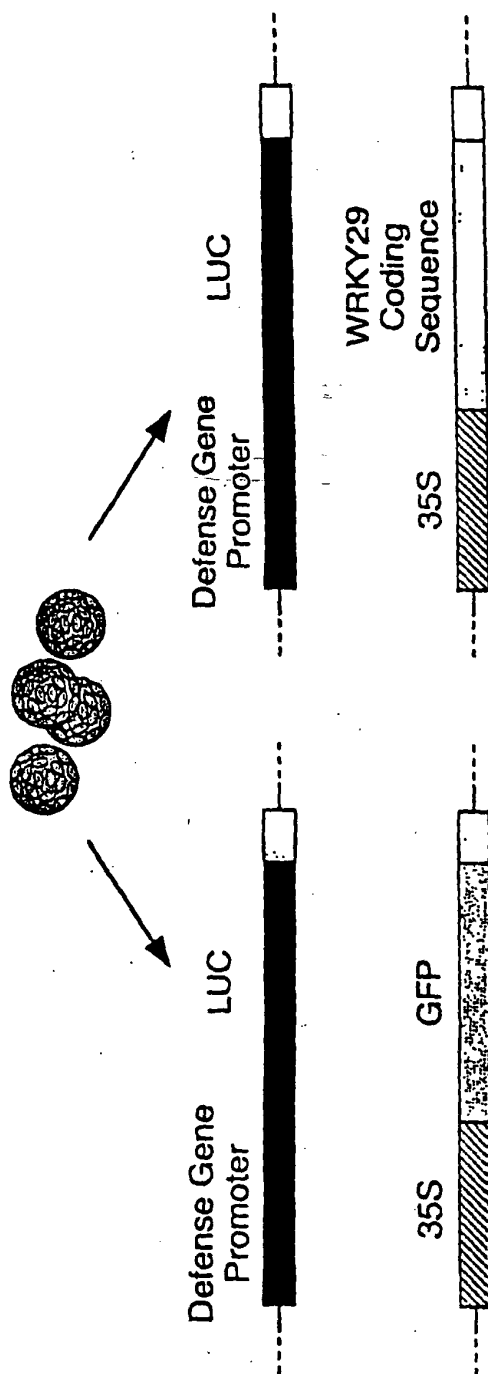
FIGURE 12

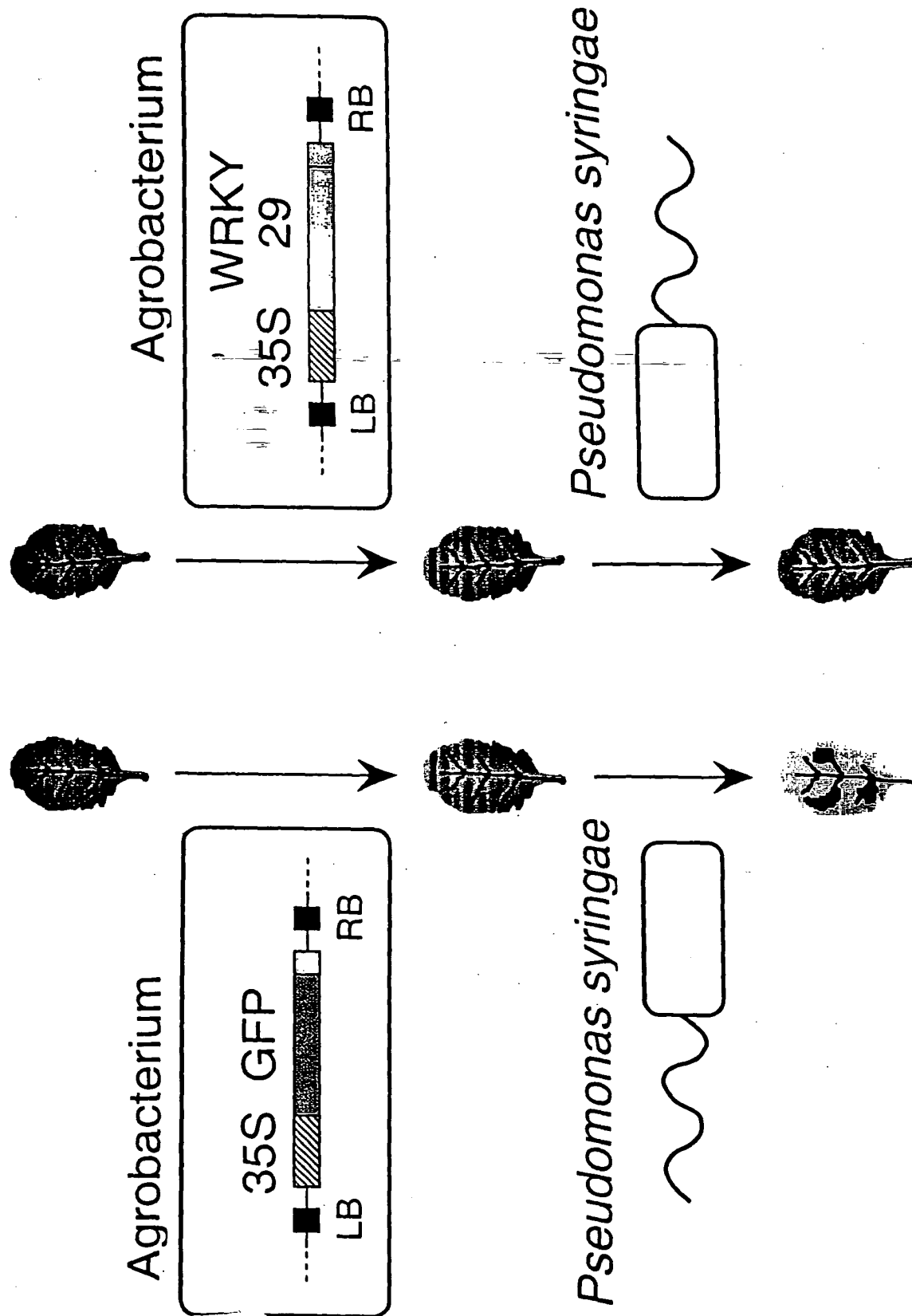# Agrobacterium-Mediated Transient Transfection

FIGURE 13

Title: MASTER ACTIVATORS OF PATHOGEN
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Serial Not: Not Yet Assigned
Customer No.: 21559

Transient Expression of WRKY29 Reduces Pathogen Susceptibility
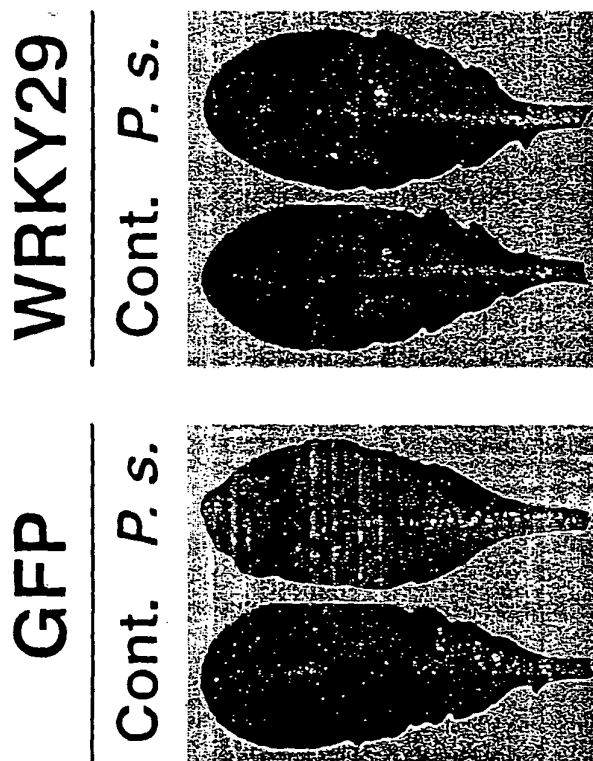
WRKY29 — Cont. *P. s.*

GFP — Cont. *P. s.*

FIGURE 14

WRKY29 promoter fragment

5'-
TCGTCCATGATGGACATATATGTGACTGCGTATTTACACACACCGCACGTATGCTTATTTCACA
CGTTAGAAGAAGAATTCAAAGAAGTCGGTTCTATTTGTATTCTTGTGAGATCATCAATATGAC
AATATCGTTCTATTAATATACGTATAATTCATATGTTGTCATGGTTTCACATACCATGTCGACA
GTCGACGTACGTACAAAAGTATAAATAGTATGAATCTAATAACAGCACCAAGATTGAAGTTC
ATCTTCTAATCAAAACTATCATAAAGTGGTTTCAAAATAGTGTTTTTTCTGATGAAACTATAAC
TGAGTTATAATCAATCCGAAATTATATAACTAATTATATTTGGGAACTAGATAAACGCAAAAA
CATGAGCAGTTTCTTATTTTTTTTGTCCAGATTTAAAATTTGGAGTGTTAAAATATACGGAGTG
TTACACAATGAAAACACAAGAAGTCAAGAACCCATAAGTTATTTTAATTAATAATATTGTATT
TAAAGTGATTATTAAAAAATAATGTAAAAACTGATTATTTGTTGACAAAAAACAGTTAGTTAT
AGTTAAATAGTATTGATGCATATATATACTATCTCATTATTTTGGTATTACTCAGTACTCACAT
CTTTAATAAAGACAAAGATAGTTAGTGTATAATTCAAATCGAACTCACAGAAGTCAATAAGC
GCGTAAAAATACAAAAATATCTGGCAGACTTTAGCAAGGTTTGTTTTCCAACAGAAATGGTCA
TTTCAGAATCATTTACATATCCATATATATAGCTCTTAAATGGTATATATTGGGTAATGGGTAT
TCGTTTAAATAATTTTGTTTTCTGTAAATTTCAAATATTAATCTGATCAGTTTATCCATGTGTGT
ATATTTAGTGTATTATCATCAATATGACATAGACAGACTTTCAAGTTGGTGCAAGAGGGGA
TGAAAATTTCTTCCCAGTTGCAAGAGTAAGCTGACTAGCATTTTTTTTTTATATATAATTTATTT
CTCAAATGGTTTTTATTATTGTTTTGTTGACTTTAAGTTTTTGCCTTTTATGGGACTGCAATCAC
CCGTGCCAACTTTTAATCTCCATCGCCTAAAAAAGAAAGAAAAGGCTACCATTATGGACCGAA
ATATTTAAGACCATAATACAAAATTATACGAATATTTTCTGTAACTTATATATATGATCATTTG
ACAAAGCAAAGTCAATCAAATAAACTTCAAAGAAATTATGAGCTTATAATAAGTTTGATAGT
GTTAAATATAATCAAATCATTAAATTTAGTATTTATTTCATCTCGGTTTCCATTTGATAGATAG
ATAAATGAAAGATAGCATCGCCAATAATGAAAAAACTTTATTTGATGGCAATACTTTGTTACA
TCATTTCTGTTTTCTTAATTTCATGTCGAAATATTGCCATGATTGTGTTCAACATAACTAGTTTT
GAGGTAACAAGTTAAAAATTTGTTATATTTTTTGAATATGTTATTCAGTTGAAAGTCATTTAGA
TGTAAGTAAAAACAAACATAAGAAGTTAACATATCAATATTAACACAGCGAATAATCATTATT
ACAAAAAAAAGCAAAAAAATAGAAGAAGATATTATATATTGGAGAATCTTTCTTTAGTCTTA
GTTGGGAAGATTTTGTGCTATGGGATTAAAGGTATCCATCCCTATTCTATGATAGAGGCGTGG
GGTTATTGGACCAATCTATATATATTACCACAAGGCTTAAGATGAAGTGATAATACAGTATTA
TTAATACCCTCCCAAATTATTTTTAAATATTTATCAAAAGAAGCTTACGGTATAGATCATACTT
GCAGCATTATTCTATAAGTTTATTTAATTTCAGTGGCTCGTTACGTGAACACAAGGTAAGCTA
ATAGACTTACGTGCCCCATTAAACACATACATAATTATACAAGTATCATGAAACTAGTGACAA
AACCTCGATCAAATAAAGAAATTACCATGACGACAAAGATAATTAAAAAAAAAAACTACTAT
ATGTCATACTCATGCATATGCATGTACAAATGCCGCTTTAAATATTTAATTTAGTTAAAGCAAT
GATATTTAAATTCTCTCTACTTCATATATATTCCAAAAGACATATTGTCAAATTCCTTTTTTTAG
TTATATATAATCATATATTCATATTGTTATATTTTCAATATTTAATAGTAAGATGGACTTTCCTG
AATGTTGTGTATGATTTATAATTTGAGATATTTTGTCGGAGATGGATATTTGACAAGTTAATGT
TACTTTATTAAAATTTTCTAAACATTTAGGTACGAATTGACTTTTTCAAAAGTCAACACAATAA
ATTTTAAAAGTTTAATGACTTAACGGGTTCACATGGGAAACGAAAACACCCTAAACCACAAA
CAATCTAATCTTATTTCCTTCTTTATATAAACCGCTGTTTCCCAAAAGGCTTGTTCTCGTCATAT
GTACTTGTACACCAACCCACCAAAAGAGATAAAAGAGGAAACAAAAACTCGAAAAGAGAGA
GATATATGGGTGAGGTGGCTTAT - 3' (SEQ ID NO.: 15)
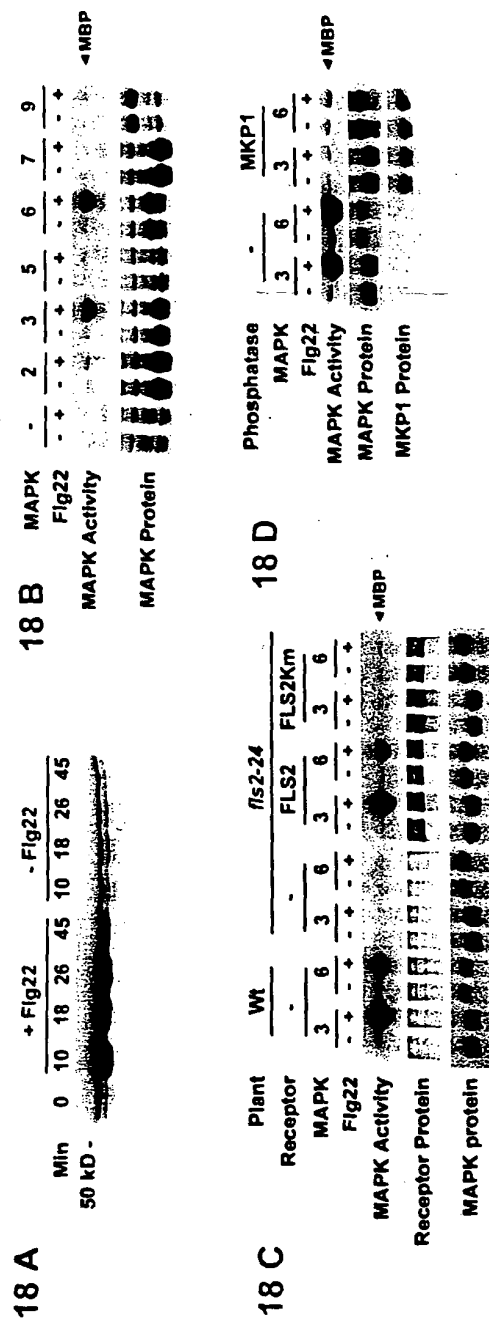
Figure 15

WRKY22 Promoter Fragment

5' -
CTGACAGTGAACTTCATTGTTCAAGCGAGGTGAGTTTCCTATTTTTCTTCTTCTCCTTTCAATTA
AAATTTCAGGGTTTATGATCTCTAGGGTTTAGGTTTTATTTTCTTAAACTAAACCCTAAATTCT
TTTTCTTCTTCTTTTTCTTGTAATTTCCAGATGCACTGCGAACGCTAGAGGAGGTGCGATATCG
AAGAGGAAGCGTTATACAGGATCATGGGACCAAAATATATCGTATAGATTCGGTTCTTGTTCT
TCTATACCTTATGAGAGTAGAAGTTTTTCTCTTCAAGAGAAAAAAAAAAAAAAAGAAAAAAAA
AAAAGAAGAGTAGAAATTTCTCTGTGTTTTTTTTTACCAACAAGACACAAATGAAACTGGTCC
AAAAGGAGTGTGTATAATCTCTGTGGAGACATAACTAATACGTTGATGAATTTCAAGAATACT
TGGATTATATAGATTAACCCTGACTCCCTTAGATAGAGATCGAAATCGGGTGGTGATTTCTGA
GACCATACAAGTTCTGATCAGATTACTACTAAGTAAATCTTAATTATTAGACTGTTTTTAATGG
ATTTTTCTGCTCTAATGATAACGTAATGAGATTTTTTTTTTTTTTTTGTATGTTTGGCTTGCAGA
CCCGGGTAATGAGAAGTTTGGTAAGAGCAAAAGGCACTAATCTCACGTAAGAAAACACTTTT
TTCATCAACCATGTATATAATCATGTCGGTTTACATAAACCGTATCGTCTATTCAAGAATTTAG
TTTTGTATAATTATAATATTTTTTTTCAGACTACTTTTCAATTAAGCATCTTTTTCTTGGATTTTTT
TTTCACAAAGGGAGAGCTTTAACTTTTTGCATTAACTTATATATTTTAAATTATACATGCATGC
ATACCGACTTATATAAATCATATGGTCAATATGAGACTTTTGATTTATATTATTTGTCAACTAA
GCATCTTTTCAGATGAGGTTCATGCACCTTTGTTAGAATTATCGGACCAGAAGATCACATCAA
CGTTTACCAAATCAACAAAAAAATCCAATCCGTCCAAAAAATTTGGAAACTGTTTGAAAGATT
CGAAATGTTGGAGCAAGGATACTCAGTTCCAATCTCTGAGCAGAATCTGATATGACTCATCTA
CTCATAAGACTTTGCGAGATAGACCGGTACAAAACCGTTTCCAAGGGTTCATAATATATGGAT
TAATGTGAGTTATTGTGGACGTTGTGGTTGTAGAAGCCGCGGTAGTCGTGGAAACACTAATTA
GTTATCTCCTGTAAGCTATTTTTATTTTTTTTCCTCACTTCCTCTTCCTCGCAGCTATGTATAATT
TTGGTTGGTTATCTCCAAAACTTTTTATGGTCAAACAATTTTGAGAAAGTAATTTGGAAAGAA
AAAAGGTTTAAGAATATCTTTTTATCGTCAAGTCCTCCTCCAAATTACTTCCTTAAAACTGTTT
GACCATAAAAAGTCATAGCAAGGTATTAGTTATTCTAATTTAAATTAAACGCCTTTTTATCAA
CAACAAAAAAAAGAAGAAGATTTGATATGTTGAAAAGTATTAGGGACGCTTATTAGGGCAGT
ATTCCTAGTTATTGCATTTTCTTTCGGTCATTCGACCTTAGGATCATACCTCAATCTGTATGACT
GTATTCGCCATGTGAATTCCAATATTACATAGTGACCAAATTTGATATCCAACTAAAAGTCGA
TCTTTGATCTAAACGAAATGACAACTATTTGGTTAGTGATTGCAGGTTGGAAAGATTTACCTTC
TAGACCTGTCTTACGAAGCTAGTATTCTAAAGTAATCTTCATAAACCGAATTCAGAAACAAAA
AAAGAAAAGGAGTCCAAAATTGTATGATCATACATTAATATCAGAATAGTCTCTTTTGTTAAA
TAAATATCTGAAGAATATATATCTCTTTGATTATTTTGTGGATGGCAATGAAACTAAGAATAT
ATATTCATTGACTTAGAAGTCGACAAAAAAAAATAAAAAAATTATTGACTTAATTACTAGTTG
ACCAATATATATATTATTAAAAGAACATATTGTATCGTTGAAAGCGGATCATCGGGTTTTAAA
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AACTCAAAAGGAAATTAGATGTGTTTTGACCATTTATTAAAATGAACCTTTTCTTGTCAAACAT
TTGAAAAATACTAGTTTTTTTTTTTGGCAACGTTGTAAATAATAGTTAAAAATAGATTTTAAGT
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TGCAGAGAATTAAAGGTAATCATTTGCCAAGGAAAAACCATGCAAATATGCAATAAGTAGAA
ATAATGTTAATGAGAGTAAGCGTTGACATATATTACGTCCTGGTCCGAACATTCTTAAAGTTG
CGTAACACTAATAACCTTAGAAGATGGTTGGTTGACTATCAACATCTTATTGACCAAATGTTTT
TTTTTTTTTAATTATAAAACAGTTGCTCATTGCTCTAGCCCAGAGAAAGCAGCTCAATTAAGTA
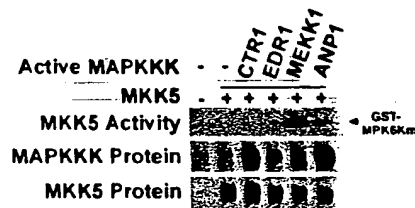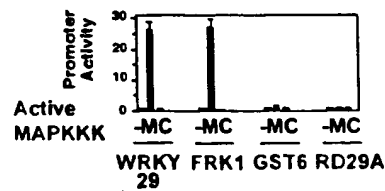A - 3'   (SEQ ID NO.:16)
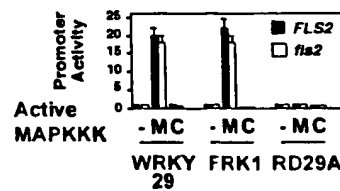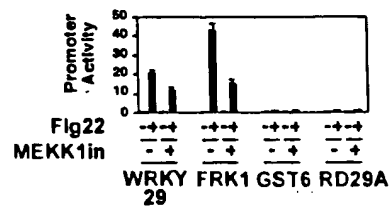
Figure 16
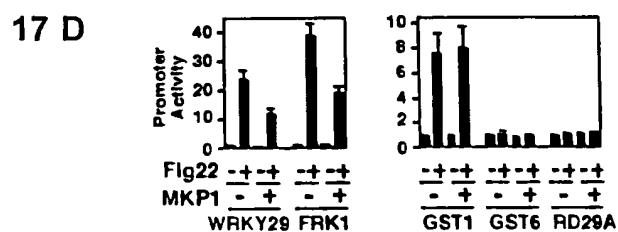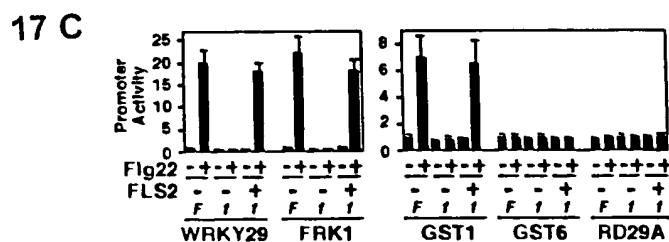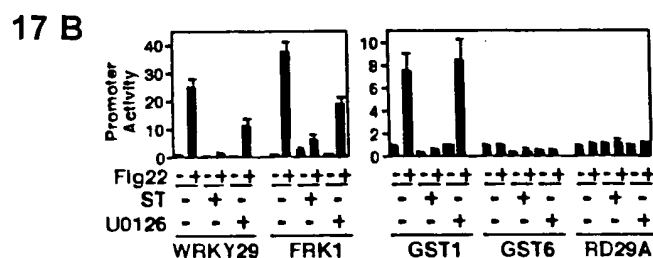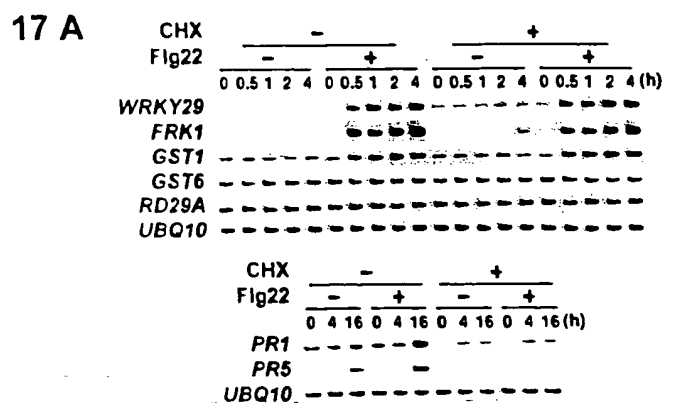
FIGURES 17 A-D

FIGURES 18 A-D

FIGURES 19 A-E

20 A

20 B

20 C

20 D

FIGURES 20 A-D

FIGURES 21 A-F

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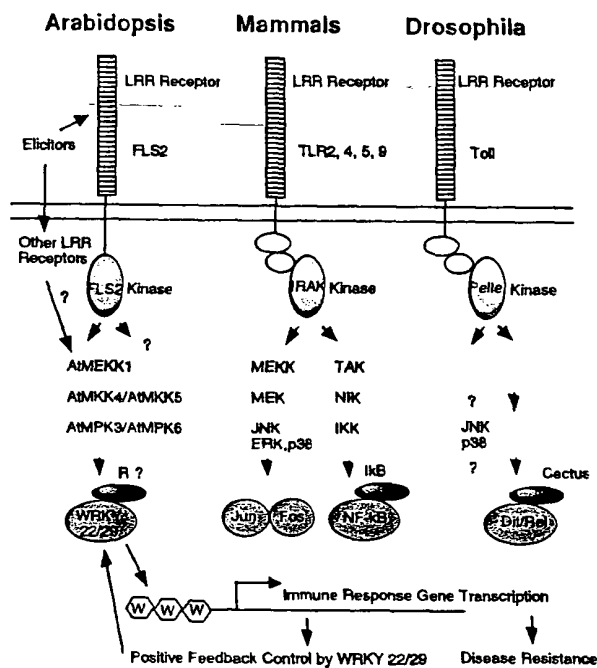Serial Not: Not Yet Assigned
Customer No.: 21559

FIGURE 22